

Appl. Serial No. 10/796,336
Response dated November 5, 2006
Reply to Office Action dated May 5, 2006

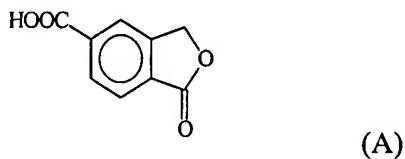
II. Amendments to the Claims

This listing of claims shall replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-21. (Canceled)

22. (Currently Amended) A process for the preparation of synthesizing citalopram and its acid addition salts, comprising synthesizing 5-carboxyphthalide of formula A

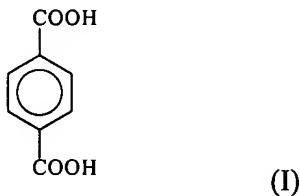


which comprises by:

reacting formaldehyde 1,3,5-trioxane of formula II:



and terephthalic acid of formula I



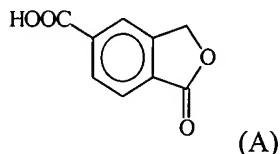
in fuming sulfuric acid containing at least 25-30% by weight of SO₃, heating the mixture at 120-135 145°C; and isolating the 5-carboxyphthalide thus obtained; and using the 5-carboxyphthalide thus obtained in a process to synthesize citalopram and its acid addition salts.

23. (Canceled)

24. (Canceled)

25. (Currently Amended) A process according to claim 22 ~~23~~, in which the 1,3,5-trioxane of formula II is used in an amount corresponding to 2.5-3.2 mol of formaldehyde/mol of the starting terephthalic acid.
26. (Original) A process according to claim 25, in which said 1,3,5-trioxane is added at a temperature of 30-35°C.
27. (Canceled)
28. (Previously presented) A process according to claim 22, in which the fuming sulfuric acid is used in an amount of 3-6 litres/Kg of terephthalic acid.
29. (Original) A process according to claim 28, in which fuming sulfuric acid is used in an amount of about 3 litres/Kg of terephthalic acid.
30. (Original) A process according to claim 22, in which 5-carboxyphthalide is isolated by neutralization of the reaction mixture with a base.
31. (Original) A process according to claim 22, in which 5-carboxyphthalide is isolated by diluting the reaction mixture with glacial acetic acid, then adding water and neutralizing with a base.
32. (Currently Amended) A process according to claim 30 ~~or 31~~, in which said base is an alkaline metal base.
33. (Original) A process according to claim 32, in which said alkaline metal base is sodium hydroxide, carbonate or bicarbonate.
34. (Original) A process according to claim 22, in which, at the end of the reaction, the 5-carboxyphthalide is isolated by the formation of a solution containing a salt thereof which is neutralized with an acid.
35. (Original) A process according to claim 34, in which said salt is the sodium salt.
36. (Original) A process according to claim 34, in which the salt is formed by adding the base to a pH of about 8.
37. (Original) A process according to claim 34, in which said acid is hydrochloric acid.

38. (Original) A process according to claim 22, in which 5-carboxyphthalide is isolated by treatment of the reaction mixture with water.
39. (Original) A process according to claim 38, in which the addition of water is made at 0-5°C and resulting exothermia is controlled by keeping the temperature at about 20-25°C.
40. (Original) A process according to claim 22, in which the mixture is heated at 130-135°C.
41. (Original) A process according to claim 22, in which formaldehyde is added to fuming sulfuric acid after the addition of terephthalic acid.
42. (Currently amended) A process for the synthesis of synthesizing citalopram, and its acid addition salts, comprising a process for synthesis of synthesizing 5-carboxyphthalide of formula A

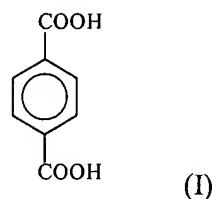


which comprises by:

reacting, in an open reactor, formaldehyde-1,3,5-trioxane of formula II:



and terephthalic acid of formula I



in fuming sulfuric acid containing at least 25-30% by weight of SO₃;

heating the mixture at 120-145°C; and

isolating the 5-carboxyphthalide thus obtained;

and using the 5-carboxyphthalide thus obtained in a process to synthesize citalopram and its acid addition salts.

43. (Canceled)

44. (Canceled)

45. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 432, in which the 1,3,5-trioxane of formula II is used in an amount corresponding to 2.5-3.2 mol of formaldehyde/mol of the starting terephthalic acid.

46. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 45, in which said 1,3,5-trioxane is added at a temperature of 30-35°C.

47. (Canceled)

48. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which the fuming sulfuric acid is used in an amount of 3-6 litres/Kg of terephthalic acid.

49. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 48, in which fuming sulfuric acid is used in an amount of about 3 litres/Kg of terephthalic acid.

50. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which 5-carboxyphthalide is isolated by neutralization of the reaction mixture with a base.

51. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which 5-carboxyphthalide is isolated by diluting the reaction mixture with glacial acetic acid, then adding water and neutralizing with a base.

52. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 50 or 51, in which said base is an alkaline metal base.

53. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 52, in which said alkaline metal base is sodium hydroxide, carbonate or bicarbonate.
54. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which, at the end of the reaction, the 5-carboxyphthalide is isolated by the formation of a solution containing a salt thereof which is neutralized with an acid.
55. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 54, in which said salt is the sodium salt.
56. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 54, in which the salt is formed by adding the base to a pH of about 8.
57. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 54, in which said acid is hydrochloric acid.
58. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which 5-carboxyphthalide is isolated by treatment of the reaction mixture with water.
59. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 58, in which the addition of water is made at 0-5°C and the exothermia is controlled by keeping the temperature at about 20-25°C.
60. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which the mixture is heated at 130-135°C.
61. (Currently amended) A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 42, in which formaldehyde is added to fuming sulfuric acid after the addition of terephthalic acid.

62. (New) A process according to claim 22 wherein the reaction mixture of 1,3,5-trioxane, terephthalic acid and fuming sulfuric acid is heated to 120°C and then the temperature of the reaction mixture is allowed to increase by spontaneous exothermia up to 130 to 135°C.
63. (New) A process according to claim 22 wherein the reaction mixture of 1,3,5-trioxane, terephthalic acid and fuming sulfuric acid is heated to 130 to 135°C if spontaneous exothermia does not occur after the reaction mixture is heated to 120°C.
64. (New) A process according to claim 42 wherein the mixture is heated at 120-135°C.
65. (New) A process according to claim 42 wherein the reaction mixture of 1,3,5-trioxane, terephthalic acid and fuming sulfuric acid is heated to 120°C and then the temperature of the reaction mixture is allowed to increase by spontaneous exothermia up to 130 to 135°C.
66. (New) A process according to claim 42 wherein the reaction mixture of 1,3,5-trioxane, terephthalic acid and fuming sulfuric acid is heated to 130 to 135°C if spontaneous exothermia does not occur after the reaction mixture is heated to 120°C.
67. (New) A process according to claim 31, in which said base is an alkaline metal base.
68. (New) A process according to claim 67, in which said alkaline metal base is sodium hydroxide, carbonate or bicarbonate.
69. (New) A process according to claim 51, in which said base is an alkaline metal base.
70. (New) A process according to claim 69, in which said alkaline metal base is sodium hydroxide, carbonate or bicarbonate.